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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/554,960	02/12/2003	David C. Kaslow	15280-3421PC	6829

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EXAMINER	
LIETO, LOUIS D	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 01/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/554,960	KASLOW ET AL.	
	Examiner	Art Unit	
	Louis D. Lieto	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *4-12 and 15-50* is/are withdrawn from consideration.

5)☐ Claim(s) *3* is/are allowed.

6)☒ Claim(s) *1,13 and 14* is/are rejected.

7)☐ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response to the Restriction requirement was received on 12/20/2005. Claims 1-50 are pending in the instant application. Applicant's election, with traverse, of group I, claims 1-5 and 13-14, in the reply filed on 12/20/2005 is acknowledged.

It is noted that in the office action of 10/21/05 the examiner's typographical error inadvertently included claims 4 and 5 in the subject matter of group I (drawn to a composition comprising an isolated nucleic acid molecule which encodes a PVS25 polypeptide and hybridizes under stringent conditions to SEQ ID NO: 3, and a method of inducing a transmission blocking immune response in a mammal, comprising administering a composition to a mammal) when they were appropriately meant to be included with the subject matter of group II (a composition comprising a PVS25 polypeptide). The corrected groups are now:

Group I, drawn to claims 1-3, 13 and 14; and Group II, drawn to claims 5-8.

Since applicant elected the subject matter of group I claims 1-3, 13 and 14 are currently under consideration.

Claims 4-12 and 15-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Response to Arguments

Applicant's election with traverse of the restriction requirement in the reply filed on 12/20/2005 is acknowledged. The traversal is on the ground(s) that the prior action of 10/21/05 failed to demonstrate a lack of unity. This is not found persuasive. Applicant argues that stringent conditions are selected to identify nucleic acids that are substantially identical to a

given sequence. However, the specification does not define stringent hybridization conditions in terms of conditions that will only work with substantially identical sequences. Instead the specification states that nucleotide sequences are substantially identical if they hybridize to each other under stringent conditions (pg. 13, lines 19-20). Finally, the specification teaches, "Stringent conditions are sequence dependent and will be different in different circumstances." (pg. 13, line 21). These conditions include those that allow sequences without substantial identity, as defined in the specification, to hybridize with each other. Therefore, under this definition the conditions necessary for the sequence taught in WO/89/19936 and SEQ ID NO:3 to hybridize could be different from those of a sequence with 80% similarity and SEQ ID NO:3, and yet still be considered stringent.

The requirement is still deemed proper and is therefore made FINAL.

Specification

The amendment filed 12/29/2003 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The specification as originally filed on 5/22/2000 does not provide support for the sequences submitted on 12/29/2003, specifically, SEQ ID NOS: 16-24.

Applicant is required to cancel the new matter in the reply to this Office Action.

Information Disclosure Statement

The references provided have been considered, but will not be listed on any patent resulting from this application because they were not provided on a separate list in compliance with 37 CFR 1.98(a)(1). In order to have the references printed on such resulting patent, a separate listing, preferably on a PTO/SB/08A and 08B form, must be filed within the set period for reply to this Office action.

Claim Objections

Claim 2 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is drawn to nucleic acids that hybridize with SEQ ID NO: 3. The claims do not require that the encoded polypeptide possess any particular biological activity, nor any particular

conserved structure, or other disclosed distinguishing feature of a Pvs25 polypeptide. Thus, the claims are drawn to a genus of nucleic acids encoding polypeptides that is defined only by the ability to hybridize under stringent conditions.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of ability to hybridize under stringent conditions. The specification teaches, "Stringent conditions are sequence dependent and will be different in different circumstances." (pg. 13, line 21). There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method

of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated nucleic acids that encode a polypeptide having the amino acid sequence set forth in SEQ ID NO: 4, but not the full breadth of the claim meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 13 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims encompass a method of inducing a transmission blocking immune response in a susceptible organism, such as a human, by administering a nucleic acid encoding a Pvs25 polypeptide.

The claims broadly encompass any route of administration. However the specification does not provide guidance on the induction of any immune response by administering a Pvs25 nucleic acid vaccine by any route. In the related field of DNA based vaccines, the route of delivery is known to have a significant effect on the efficiency of expression. McCluskie et al. teaches that the route of delivery of DNA vaccine influences immune responses in laboratory animals {McCluskie et al. (1999) Mol. Med. 5:287-300; Abstract}. Specifically, in one study McCluskie et al. only observed antibody responses to injected routes of administration of DNA vaccines and not to non-injected injected routes of administration of DNA vaccines, such as oral routes, sub lingual, inhalation and vaginal wall because of variation in transfection efficiency (Abstract). The specification does not provide any guidance on the specific efficacy of any routes of administration of the claimed vaccine to induce a transmission blocking immune response.

Further, the specification as filed does not provide any guidance on the ability of a nucleic acid encoding a Pvs25 polypeptide to induce any transmission blocking immune response. Example 6 discusses an *in vitro* method of assessing transmission-blocking activity of anti-sera generated from mice immunized by intraperitoneal injection of Pvs-25 or Pvs-28 polypeptides. However, the example does not describe any results of the analysis, such as whether the Pvs-25 or Pvs-28 polypeptides were successful at inducing transmission blocking activity as analyzed by the assay of example 6. Finally, the specification does not provide any guidance on the ability of a nucleic acid encoding a Pvs25 polypeptide to induce any immune response in any susceptible/model organism, such as mouse or a human. The specification does not provide any guidance on the minimum amount of nucleic acid encoding a Pvs25 polypeptide that must be administered in order to induce an immune response.

Additionally, the specification does not teach the timing, routes of administration, dosage, or levels of protein expression required in order to induce transmission blocking response of any nucleic acid vaccine encoding a Pvs25 polypeptide. Further, the specification does not provide guidance on any nucleic acids, other than SEQ ID NO:3, that encode a Pvs25 polypeptide and can be targeted use as a nucleic acid vaccine. In 2004, the art of record reported that a potent immune response was generated in mice with a DNA vaccine construct encoding a Pvs25 polypeptide fused at the amino terminus with tissue plasminogen activator signal peptide {Kongkasuriyachi et al. (2004) Vaccine 3205:3213, Abstract}. However, neither the priority documents nor the specification as filed provide any guidance on the administration of a Pvs25 polypeptide fused at the amino terminus with tissue plasminogen activator signal peptide.

The problems of DNA vaccines designed to induce an immune response against parasites are numerous. Kofta et al. reported that DNA vaccines have vast differences inefficiency when administered to different strains of mice and rats {Kofta et al. (2001) Vet Parasitology 100:3-12; pg. 7, pgph 4-5}. Kofta reports that when anti-plasmodium DNA vaccines were administered to six different strains of mice produced very different levels of protection, ranging from none to very high (pg. 7, pgph 5). Similarly, it was observed that when the same F. hepatica DNA vaccine was administered to two different strains of rats, protection was observed in only one strain. Further, Kofta teaches that the route of administration of DNA vaccines is very important at producing an immune response, and that the optimal route differs between species for the same vaccine (pg. 6; Section 1.2). Kofta teaches that a Plasmodium DNA vaccine was effective at inducing an antibody response in mice, when administered intramuscularly, but was ineffective when administered to monkeys via the same route. Kofta

concludes by stating that the whole picture of DNA vaccination against parasitic infections remains unclear, and much more research into areas such as DNA vaccines in specific target species of animals (pg. 10).

Therefore, given the lack of guidance in the specification on the ability of any nucleic acid encoding a Pvs25 polypeptide to induce a transmission blocking immune response in any susceptible organism, and the lack of teachings in the art, the skilled practitioner would be unable to predict how to practice the invention as claimed without extensive and undue experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by WO 89/10936 (16.11.89), hereafter referred to as Miller et al.

Miller et al. provides guidance on an isolated gene encoding Pfs25 (pg. 9, lines 31-33, Fig. 1, claim 2). Tsuboi et al. teaches that the nucleic acid sequences of Pfs25 and Pvs25 encode proteins with a 45% identity (Tsuboi et al. (1998) Mol. Med. 12:772-782 ; Table 1). Therefore, given that the specification's definition of hybridization under stringent conditions is defined as "sequence dependent and will be different in different circumstances." (pg. 13, line 21), it is inherent that conditions exist for these two sequences that allow them to hybridize with each

other. Therefore, by teaching all the limitations of the claims as written, Miller et al. clearly anticipates the instant invention as claimed.

Examiner's Comment

Further pertinent art of record is exemplified by Tsuboi et al. (1998) Mol. Med. 12:772-782. Tsuboi et al. teaches a sequence of Pvs25, with the exact same sequence as SEQ ID NO :3. However the reference of Tsuboi et al. was published after the filing date of the provisional application 60/067,596 (12.05.97) and therefore does not qualify as prior art under the relevant statutes.

Claims 1, 2, 13, and 14 are not allowed.

Claim 3 is allowable.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on

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